

1 **Clinical characteristics of pregnant women with COVID-19 in Japan: a nationwide**
2 **questionnaire survey**

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5 **Short running title: Pregnant women with COVID-19 in Japan**

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1 **Abstract**

2 **Objective:** To describe the clinical characteristics and outcomes of pregnant women
3 with coronavirus disease (COVID-19) on a national scale in Japan.

4 **Design:** A nationwide questionnaire-based survey forwarded to all 2185 maternity
5 services in Japan.

6 **Setting:** A total of 1418 obstetric units that responded (65% of all delivery institutions
7 in Japan).

8 **Population:** Pregnant women with COVID-19 diagnosed between January and June
9 2020.

10 **Methods:** Data were extracted from the questionnaire results.

11 **Main outcome measures:** Incidence of pregnant women with COVID-19 and infant
12 infection, positive rate of the universal screening test for asymptomatic pregnant
13 women, identification of infection route, and rates of maternal death, severe cases, and
14 caesarean sections.

15 **Results:** Seventy-two pregnant women were reported to be diagnosed with COVID-19.
16 The positive rate of the universal screening test for severe acute respiratory syndrome
17 coronavirus 2 (SARS-CoV-2) for asymptomatic pregnant women was 0.03% (2/7428).
18 The most common route of infection was familial (57%). Fifty-eight pregnant women
19 with COVID-19 were symptomatic; of whom five (8.6%) had a severe infection and

1 one patient died (a tourist). Severe respiratory symptoms, oxygen administration, and
2 pneumonia were frequently reported in the third trimester and postpartum period
3 compared to early pregnancy (22.2% vs. 2.5% [$p=0.03$], 38.9% vs. 7.5% [$p=0.01$], and
4 50.0% vs. 7.5% [$p<0.01$], respectively). All pregnant women with COVID-19
5 underwent caesarean section, regardless of symptoms. There was no SARS-CoV-2
6 transmission to the newborns.

7 **Conclusion:** The importance of infection prevention should be emphasized, especially
8 in pregnant women, their families, and their roommates during late pregnancy.

10 **Funding:** This nationwide survey associated with COVID-19 is supported by Japan
11 Association of Obstetricians and Gynecologists (JAOG).

13 **Tweetable abstract:** Prevention of SARS-CoV-2 infection is important for pregnant
14 women and their families, especially in late pregnancy.

16 **Keywords:** COVID-19; pregnancy; delivery

1 **Introduction**

2 The World Health Organization (WHO) declared the coronavirus disease (COVID-19)

3 outbreak as a pandemic in March 2020.¹ In Japan, the first case of COVID-19 was

4 reported on January 16, 2020.² In response to the spread of infection, the Japanese

5 government began conducting polymerase chain reaction (PCR) testing for severe acute

6 respiratory syndrome coronavirus 2 (SARS-CoV-2) on all patients with fever and

7 respiratory symptoms or those who had been in close contact with infected people. On

8 April 7, a state of emergency was declared, which lasted until May 25, in which schools

9 were closed, business activities were suspended and external movements for non-

10 essential reasons were prohibited. As a result, the first wave of infections in Japan,

11 which began in early April, was over by the end of June.³

12

13 For respiratory viral infections such as influenza, pregnant women are known to be at a

14 higher risk for severe illness^{4,5}, where the risk is highest in later pregnancy.⁴ However,

15 it is not known if SARS-CoV-2 infections show a similar trend. Although the number of

16 cases of COVID-19 is increasing worldwide, clinical features of COVID-19 in pregnant

17 women remain unknown. To date, reports have been case series, with very few studies

18 that have examined pregnant women throughout pregnancy at a national scale.⁶

1 Therefore, most studies have not presented an overview of pregnant women with
2 COVID-19 across an entire country and throughout pregnancy. We investigated the
3 characteristics and outcomes of pregnant women with COVID-19 in Japan and utilized
4 the findings to propose future prevention and treatment strategies.

6 **Methods**

7 The Japan Association of Obstetricians and Gynecologists (JAOG) conducted a
8 nationwide survey examining the effects of COVID-19 on maternity services. The
9 nationwide questionnaire-based survey was conducted between July and August 2020. A
10 questionnaire, with a cover letter outlining the purpose of the study, was mailed to the
11 Director or the Chief obstetrician in foetal-maternal medicine of all 2185 delivery
12 institutions in Japan. Survey responses were received via a web form. The questionnaire
13 consisted of two parts: a standard questionnaire and a detailed questionnaire. The
14 standard questionnaire included questions on the number of pregnant and postpartum
15 women with COVID-19 that were being managed within each unit, as well as, whether
16 universal testing of asymptomatic pregnant women had been performed between
17 January 16 and June 30, 2020. In instances where a pregnant woman with COVID-19
18 was reported, the detailed questionnaire investigated the maternal characteristics, course

1 of onset, symptoms, epidemiological history, clinical course, and maternal and perinatal

2 outcomes of each case. All patient data were anonymized.

3

4 A confirmed case of COVID-19 was defined as having a positive real-time reverse

5 transcriptase (RT)-PCR SARS-CoV-2 assay from nasal and pharyngeal swab specimens

6 or as having respiratory compromise in the presence of characteristic radiographic

7 changes of COVID-19. Pregnant women with a history of symptoms or potential

8 exposure to COVID-19 were tested for SARS-CoV-2. In some hospitals, universal

9 screening of all pregnant women was performed. Nasal and pharyngeal swabs were

10 obtained from almost all newborns born to infected mothers and the samples were

11 subsequently tested using RT-PCR. Computed tomography (CT) of pregnant women

12 was performed at the discretion of the doctor, with pneumonia being diagnosed based

13 on the CT findings.

14

15 Pregnant women with COVID-19 were categorized as symptomatic or asymptomatic,

16 based on the presence or absence of symptoms prior to admission and during

17 hospitalization. The severity of disease was defined as severe or critical. Severe cases

18 were defined as cases with severe respiratory symptoms (having one of the following:

1 respiratory rate $>30/\text{min}$; percutaneous oxygen saturation $<93\%$; or ratio of arterial
2 oxygen partial pressure to inspired oxygen fraction <300).⁷ Critical cases were defined
3 as those requiring admission to the intensive care unit (ICU) or having respiratory
4 failure and requiring mechanical ventilation.

6 **Statistical analyses**

7 Data were analysed using IBM SPSS Statistics for Mac, version 25.0 (IBM Corp.,
8 Armonk, N.Y., USA). Nonparametric continuous variables were compared using the
9 Mann–Whitney U test. Categorical variables were compared using the chi-squared test
10 and Fisher’s exact test. Statistical significance was defined as P -value <0.05 .

12 **Funding**

13 This nationwide survey associated with COVID-19 is supported by JAOG. The funder
14 had no role in study design, data collection, data analysis, data interpretation, or the
15 writing of the report.

17 **Results**

18 Questionnaires were sent to 2185 medical facilities with maternity services. Responses
19 were received from 1418 (64.9%) facilities, that had previously recorded a total number

1 of 611,444 deliveries in 2019 (71.1% of all deliveries in Japan). The positive rate of the
2 universal SARS-CoV-2 screening of asymptomatic pregnant women during the study
3 period was 0.03% (2/7428).

4

5 Seventy-four pregnant women with confirmed COVID-19 were treated in 48
6 institutions between 16 January and 30 June, 2020. Of these, one case was a duplicate
7 record and another had missing data. Hence, 72 women with complete data were
8 included in this analysis; of which 58 (80.6%) were symptomatic and 14 (19.4%)
9 asymptomatic.

10

11 The maternal characteristics of patients with COVID-19 are shown in Table 1. The
12 median maternal age of symptomatic and asymptomatic patients were 31 (interquartile
13 range (IQR), 27–36) and 32 (25–33) years, respectively. Among the asymptomatic
14 patients, 85.7% had been tested after having been in contact with confirmed or
15 suspected individuals and 14.3% were tested during universal screening. The majority
16 of symptomatic patients were diagnosed during the second trimester (46.6%), while the
17 majority of asymptomatic patients were diagnosed during the third trimester (35.7%). In
18 both groups, the most common route of infection was familial (56.9% for symptomatic

1 patients and 57.1% for asymptomatic patients). Only one asymptomatic patient (1.7%),
2 a tourist from Europe, died due to COVID-19.

4 The maternal clinical presentation of symptomatic COVID-19 patients is shown in
5 Table 2. The most common symptoms were fever (70.7%) and cough, respiratory
6 distress, or sore throat (67.2%). Five patients (8.6%) had severe respiratory symptoms.
7 Seventeen women (32.8%) underwent a chest CT scan during pregnancy, and 12 had
8 radiologically confirmed pneumonia (20.9%). Forty-eight (82.8%) were hospitalized
9 and the time from symptom onset to hospitalization was a median of 6 days (IQR, 2–
10 10). Ten women (17.2%) required oxygen administration and three (5.2%) were
11 admitted into the ICU. One woman (1.7%) needed mechanical ventilation and she died.

13 A total of 24 infected women delivered infants during the study period. Of these, 12
14 deliveries occurred during active infection and the others occurred after recovery.

15 Perinatal outcomes of COVID-19 patients who delivered during infection are shown in
16 Table 3. Nine of the women were symptomatic and three were asymptomatic. All 12
17 underwent caesarean section, with 11 of them performed due to concerns about the
18 effects of COVID-19 on pregnancy. All 12 women delivered live infants, and no severe

1 neonatal asphyxia was observed. Eleven newborns were tested for SARS-CoV-2 using
2 nasal and pharyngeal swabs and all the infants tested negative. None of the infants born
3 to these women suckled; one infant was fed breastmilk through milking, while the
4 others were fed formula milk. In all the cases, the mother and baby were separated
5 while being managed. The maternal outcomes of symptomatic patients in each
6 pregnancy period are shown in Table 4. Severe respiratory symptoms, oxygen
7 administration, and radiologically confirmed pneumonia were frequently reported in the
8 third trimester and postpartum period compared to in early pregnancy (22.2% vs. 2.5%
9 [p=0.03], 38.9% vs. 7.5% [p=0.01], and 50.0% vs. 7.5% [p<0.01], respectively).

10

11 **Discussion**

12 **Main Findings**

13 In this nationwide survey conducted in Japan, 72 COVID-19 cases were reported among
14 pregnant women and the positive rate of the universal SARS-CoV-2 screening test of
15 asymptomatic pregnant women was 0.03%. The most common route of infection was
16 familial (57%). Severe respiratory symptoms, oxygen administration, and pneumonia
17 were more commonly observed during late pregnancy than in early pregnancy;
18 suggesting that COVID-19 may potentially be more severe during late pregnancy. All

1 pregnant women infected with COVID-19 underwent caesarean section and no SARS-
2 CoV-2 transmission was detected in the newborn. Five-percent of infants were
3 breastfed, regardless of symptoms.

4

5 **Strengths and Limitations**

6 A major strength of this study is that it was the first rapid nationwide questionnaire
7 survey of pregnant women with COVID-19 in Japan. Therefore, the results are
8 extremely valuable for understanding the current situation of infection and determining
9 future measures in Japan. A limitation is that the analysis was based on a questionnaire
10 survey that asked for experiences and clinical courses associated with COVID-19. We
11 do not collect detailed data, such as racial background, blood test results or changes in
12 symptoms before and after delivery. The response rate for this rapid survey was 65%,
13 but the total number of cases is underestimated and the overall incidence is
14 approximate, because we do not have the complete number of infected patients. It is
15 necessary to build a national surveillance system for prospective observation.

16

17 **Interpretation**

18 Seventy-two pregnant women with COVID-19 diagnosed in the medical facilities
19 between January 16 and June 30 were reported. There were approximately 305,722

1 deliveries in the aforementioned 6-month period in the institutions that participated in
2 this survey. Therefore, the estimated incidence rate over the study period was 23.6 per
3 100,000 pregnant women. The prevalence of COVID-19 among asymptomatic pregnant
4 women during the study period was 0.03% (2/7428), which is much lower than the
5 prevalence reported in the United States (1.5%⁸ and 13.7%).⁹ The prevalence in
6 asymptomatic pregnant women was as low as the estimated incidence rate, suggesting
7 that there was no strong benefit to the screening tests. With the noted prevalence,
8 expansion of the PCR testing system for symptomatic pregnant women should be a
9 priority. We believe that this approach may also be useful in preventing nosocomial
10 infections.

11

12 According to a study, most pregnant women, in the United Kingdom, are admitted to the
13 hospital with COVID-19 symptoms in the third trimester or during peripartum.⁶

14 Additionally, a report from Spain found that the proportion of women with symptoms
15 and those requiring hospitalization was higher among women in the third trimester.¹⁰

16 Maternal physiological adaptation of cardiovascular and respiratory systems during
17 pregnancy and the associated immunological changes may result in reduced tolerance to
18 respiratory infections and pneumonia during pregnancy, especially in the later stages.^{11,}

1 ¹² Our results, along with these reports, suggest that pregnant women with COVID-19
2 may experience more severe symptoms in the third trimester and during postpartum.
3 Therefore, both pregnant women and healthcare providers need to be more cautious
4 about COVID-19 during late pregnancy than in early pregnancy. In the present study,
5 the time from symptom onset to hospitalization was 6 days, with peak symptoms on the
6 day of admission. Shortening the duration from onset of symptoms to hospitalization
7 may allow interventions especially in late pregnancy.

9 Nearly 60% of the cases were diagnosed or suspected to have a familial infection. It is
10 possible that the emergency declaration by the Japanese government led to a reduction
11 in outdoor person-to-person contact, which may have led to more pronounced familial
12 infections. According to public data on the status of infection in Tokyo, which has the
13 highest number of infected people in Japan, the proportion of pregnant women among
14 all infected people from April to August 2020 was 0.53%; the proportion of pregnant
15 women in the population of Tokyo in 2020 is estimated to be 1.89%. The proportion of
16 pregnant women in the infected population is more than one-third lower than the
17 proportion of pregnant women in the population. Therefore, it is presumed that pregnant
18 women are taking appropriate measures to prevent infection. Under these

1 circumstances, to prevent familial infection as a further infection control measure, not
2 only pregnant women but also their families and roommates need to be vigilant with
3 infection prevention. To prevent familial clusters, isolation should be considered if
4 someone in the family has symptoms or has been in contact with confirmed or suspected
5 COVID-19 patients.

7 Although there was no SARS-CoV-2 transmission to the newborns, all pregnant women
8 with COVID-19 delivered via caesarean section, regardless of their symptoms. It has
9 been suggested that presence of COVID-19 alone is not an indication for caesarean
10 section and that the mode of delivery should follow obstetric indications.¹³ Ferrazzi et
11 al. proposed that vaginal delivery is appropriate in mild cases and that caesarean section
12 should be planned in severe cases.¹⁴ In addition, caesarean delivery has been reported to
13 be associated with an increased risk of clinical deterioration.¹⁵ Owing to few facilities
14 with negative pressure delivery rooms in Japan, the JSOG has stated that caesarean
15 section may be selected for the purpose of shortening labour time, simultaneously
16 securing medical resources, and preventing mother-to-child transmission.¹⁶ This
17 statement may have greatly influenced the choice of caesarean section during the study
18 period, which was in the early stages of managing COVID-19 in pregnant women in

1 Japan. Currently, an increasing number of facilities have changed policies and are now
2 opting for vaginal deliveries. The mode of delivery should be individually determined,
3 depending on the maternal conditions.

4 Breast milk was administered through milking in only one asymptomatic case. The
5 JSOG recommends the use of artificial milk because the breast milk could possibly
6 contain the virus.¹⁶ On the other hand, it has been suggested that SARS-CoV-2 is
7 unlikely to infect newborns via breast milk and WHO recommends that mothers with
8 suspected or confirmed COVID-19 should be encouraged to initiate or continue
9 breastfeeding.¹⁷ Further investigations are needed on breastfeeding of mothers with
10 COVID-19.

11

12 **Conclusion**

13 In Japan, the number of cases of COVID-19 in pregnant women is very low. Our result
14 does not indicate that pregnant women are more likely to become severely ill, but it
15 does indicate that late pregnancy may be a risk factor for exacerbation of the symptoms
16 compared to early pregnancy and that familial transmission is the most common route
17 of infection.

1 **Disclosure of interests**

2 None reported.

3

4 **Acknowledgements**

5 We are grateful to the doctors who answered the present questionnaire survey.

6 Members of Department of Medical Safety, the Japan Association of Obstetricians and

7 Gynecologists (JAOG): Tomoaki Ikeda (Chair), Koyo Yoshida, Isamu Ishiwata,

8 Akihiko Sekizawa, Yasushi Kuribayashi, Shunji Suzuki, Kazuhiko Ochiai, Hirokatsu

9 Kitai, Kentaro Shimura, Kaoru Kimura, Ken Ishitani, Junichi Hasegawa, Masaji

10 Nagaishi, Tatsuya Arakaki, Gen Ishikawa, Susumu Oka, Osamu Samura, Hiroaki

11 Tanaka, Hiroshi Ishikawa, Takao Kobayashi, Yasumasa Ohno, Kayo Osada, Yukiko

12 Kawana, Hiroyuki Seki, Masahiko Nakata, Koji Hashii, Satoshi Hayashi, and Takeshi

13 Murakoshi.

14 President of JAOG: Katsuyuki Kinoshita

15

16 **Contribution to authorship**

17 TA, JH, and AS conceived the study. TA, JH, and AS drafted the initial protocol,

18 analysed the data, and wrote the first draft of the manuscript. All authors collected data.

19 TA, JH, AS, and II coordinated the study, and with TA, JH, and AS developed the

1 database and analysed the data. All authors contributed towards drafting the manuscript.

2 II, TI, and KK are the guarantors of the study. All authors had full access to study data

3 and take responsibility for the integrity of the data and the accuracy of data analysis.

4

5 **Details of ethics approval**

6 This study was approved by the Japan Association of Obstetricians and Gynecologists

7 (No. 294, July 12, 2020). This investigation was conducted in accordance with the

8 principles of the Declaration of Helsinki. All patient records and data were anonymized

9 by the institutions prior to submission for analyses. Therefore, the requirement to obtain

10 informed consent was waived, therefore, informed consent was not obtained from the

11 participants or their families.

12

13 **Funding**

14 This nationwide survey associated with COVID-19 is supported by JAOG. The funder

15 had no role in study design, data collection, data analysis, data interpretation, or the

16 writing of the report.

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